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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/715,764	11/15/2000	Heinz-Josef Lenz	13761-0739	7045

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EXAMINER
ZITOMER, STEPHANIE W

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 08/27/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/715,764	Applicant(s) LENZ ET AL.	
	Examiner Stephanie Zitomer	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 March 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *35-60* is/are pending in the application.

4a) Of the above claim(s) *35-46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *47-60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Application status

1. Receipt of the Amendment and Response filed March 1, 2002 is acknowledged.

2. Objections and rejections not reiterated herein from the previous Office action, paper no. 5 mailed August 1, 2001, have been withdrawn in view of applicant's cancellation of claims 1-34. Arguments set forth in the Amendment and Response filed March 1, 2002 have been fully considered but are deemed moot in view of withdrawal of the previous rejections and new grounds for rejection.

Informalities

3. The disclosure is objected to because of the following informalities: the word "thymidylate" is misspelled in the claims and throughout the specification.

Appropriate correction is required.

Election by original presentation

4. Newly submitted claims 35-46 are directed to an invention that is independent or distinct under 35 U.S.C. 121 from the invention originally claimed for the following reasons:

Invention I, original claims 1-34, is directed to a method for determining effectiveness of a therapeutic regimen, classified in class 435, subclass 6.

Invention II, new claims 35-46, is directed to a method for treatment of cancer, classified in class 514, subclass 44.

Inventions I and II are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, firstly, the inventions are not disclosed as capable of use together because the specification does not describe how to perform the claimed method for treatment of cancer. Secondly, the method of Invention I requires determining the potential effectiveness of a therapeutic regimen for future use by assaying a genomic polymorphism in a subject with cancer whereas in Invention II a chemotherapeutic drug is administered to a subject after selection of the drug based on assay of a genomic polymorphism. Thus the inventions require different method steps, have different functions and modes of operation and have different effects. In view of these differences and their recognized divergent subject matter

as evidenced by their separate classification searches for Inventions I and II would not be coextensive. Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 35-46 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03. New claims 47-60, which are drawn to the same subject matter as the original claims, are presently under prosection.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Rejections under 35 U.S.C. 112, second paragraph: Indefiniteness

5. Claims 47-60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) The term "suitability" in claims 46-56 is a relative term which renders the claim indefinite. The term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is suggested to recite a relationship between "suitability of treating" and "the response of the subject to said chemotherapeutic drug". As written, the latter phrase lacks antecedent basis in the claim context.

(b) Regarding claim 59, the phrase "or the like" renders the claim indefinite because the claim includes elements not actually disclosed (those encompassed by "or the like"), thereby rendering the scope of the claim unascertainable. See MPEP § 2173.05(d).

(c) Claims 57-60 are written in such general terms which are not particular to "screening for the effectiveness of TS directed drug therapy" that the "instructions for use of the kit" are *non sequitur*. It is unclear what method(s) is contemplated to be performed such that one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Rejection under 35 U.S.C. 102(b): Anticipation

6. Claims 47-49 are rejected under 35 U.S.C. 102(b) as being anticipated by Leichman et al. (1997) (J. Clin. Oncol. 15(10):3223-3229) taken with Horie et al. (1995) (Cell Struct.

Funct. 20:191-197). Leichman et al. disclose the claimed method for determining the suitability of treating a cancer in a subject with a chemotherapeutic drug comprising taking a biological sample (colorectal cancer biopsy) of a subject and using the sample to determine the intratumoral expression of the TS gene which determined the response of the subject (page 3226, last paragraph). The recitation in claim 47, "to determine the genotype of a gene of a subject" is inherent in the reference method because it was known in the art that the genotype of the TS gene determined the expression as taught, for example, by Horie et al. (abstract, last three lines).

Rejections under 35 U.S.C. 103(a): Obviousness

7. Claims 47-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Leichman et al. (1997) (J. Clin. Oncol. 15(10):3223-3229) in view of Horie et al. (1995) (Cell Struct. Funct. 20:191-197). Regarding claims 47-49, Leichman et al. disclose the claimed method for determining the suitability of treating a cancer in a subject with a chemotherapeutic drug comprising taking a biological sample (colorectal cancer biopsy) of a subject and using the sample to determine the intratumoral expression of the TS gene which determined the response of the subject (page 3226, last paragraph). The recitation in claim 47, "to determine the genotype of a gene of a subject" is inherent in the reference method because it was known in the art that the genotype of the TS gene determined the expression as taught, for example, by Horie et al. (abstract, last three lines).

Regarding claim 50, Horie et al. determined the genotype of the TS gene wherein the TS gene has a 28 bp tandem repeat in the 5' UR. (page 194, Figure 4) which is polymorphic in the number of repeats, two or three, in human subjects (abstract). It would have been known to one of ordinary skill in the art at the time the claimed invention was made that TS genotypes included homozygous for a triple repeat, heterozygous for a triple and a double repeat and homozygous for a double repeat based on general knowledge in the art of the presence of two copies or alleles of each gene in human subjects.

Regarding claims 51-54, Leichman et al. disclose the chemotherapeutic TS directed drug, 5-fluorouracil, a fluoropyrimidine, and human subjects (abstract).

Regarding claims 55 and 56, Leichman et al. extracted TS mRNA for direct determination of TS expression by RT-PCR (page 3224 at "Laboratory Methods"). However,

one of ordinary skill in the art would have been motivated to determine genotype by analyzing genomic DNA instead of mRNA as in the references for the known benefit of reducing the time, labor and cost of the analyses. Analysis of PCR products by electrophoresis was routinely practiced in the art.

8. Claims 57-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Leichman et al. (J. Clin. Oncol. 15(10):3223-3229) (1997) in view of Horie et al. (1995) (Cell Struct. Funct. 20:191-197) as applied to claims 447-56 above and further in view of routine practice in the art. The claimed invention differs from the teachings of Leichman et al. and Horie et al. wherein means for determining a genomic polymorphism of the TS gene for use in screening for the effectiveness of TS directed drug therapy in human subjects are provided in a kit including instructions for use and wherein all or some of the positive and negative controls, primers, sequencing markers and probes for determining the presence of a tandemly repeated 28 base-pair nucleic acid sequence that defines the genomic polymorphism in the 5' UTR of the TS gene in solution or as a dispersion are included. However, the skilled practitioner in the art would have been motivated to provide the reagents, controls and polymorphic DNA of Horie et al., especially the DNA tandemly repeated sequences, in a kit in view of routine practice in the art and of the teachings of Leichman et al. of the relationship between the TS polymorphism and the effectiveness of chemotherapy for the known benefits of ease of use and commercial applications.

Conclusion

9. No claim is allowed.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action.

In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephanie Zitomer whose telephone number is (703) 308-3985. The examiner can normally be reached on Monday through Friday from 9:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152. The official fax phone number for this Group is (703) 308-4242. The unofficial fax number is (703) 308-8724. The examiner's Rightfax number is 703-746-3148.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196. For questions and requests relating to formal matters contact Patent Analyst Tiffany Tabb at 703-605-1238.

S. Zitomer
Stephanie Zitomer, Ph.D.
August 26, 2002

STEPHANIE W. ZITOMER
PRIMARY EXAMINER